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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,880	07/10/2003	Benjamin David Silverman	YOR920030162US1	2640
48062	7590	08/05/2008		
RYAN, MASON & LEWIS, LLP			EXAMINER	
1300 POST ROAD			NEGIN, RUSSELL, SCOTT	
SUITE 205				
FAIRFIELD, CT 06824			ART UNIT	PAPER NUMBER
			1631	
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			08/05/2008	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/616,880	<b>Applicant(s)</b> SILVERMAN, BENJAMIN DAVID
	<b>Examiner</b> RUSSELL S. NEGIN	<b>Art Unit</b> 1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### **Status**

- 1) Responsive to communication(s) filed on 07 May 2008.
- 2a) This action is FINAL.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### **Disposition of Claims**

- 4) Claim(s) 1,3-5,7-9,14,15,17 and 19-21 is/are pending in the application.
  - 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1,3-5,7-9,14,15,17 and 19-21 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### **Application Papers**

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.
 

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### **Priority under 35 U.S.C. § 119**

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### **Attachment(s)**

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/SB/08)
 

Paper No(s)/Mail Date \_\_\_\_\_
- 4) Interview Summary (PTO-413)
 

Paper No(s)/Mail Date \_\_\_\_\_
- 5) Notice of Informal Patent Application
- 6) Other: \_\_\_\_\_

**DETAILED ACTION**

***Comments***

Applicants' amendments and request for reconsideration in the communication filed on 7 May 2008 are acknowledged and the amendments are entered.

Claims 1, 3-5, 7-9, 14-15, 17, are 19-21 are pending, and examined in this Office action.

***Claim Rejections - 35 USC § 101***

The following 35 U.S.C. 101 Rejections are reiterated from the previous Office:

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 3-5, 7-9, 14-15, 17, and 19-21 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The following analysis of facts of this particular patent application follows the analysis suggested in the "Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility". Note that the text of the Guidelines is italicized.

To satisfy section 101 requirements, the claim must be for a practical application of the § 101 judicial exception, which can be identified in various ways (Guidelines, p. 19):

- The claimed invention "transforms" an article or physical object to a different state or thing.
- The claimed invention otherwise produces a useful, concrete and tangible result.

In the instant case, the claimed invention does not "transform" an article or physical object to a different state or thing because it is a method for calculating a global hydrophobic moment of a tertiary protein structure. This does not preclude the subject matter to be patentable as, for eligibility analysis, as

*physical transformation "is not an invariable requirement, but merely one example of how a mathematical algorithm [or law of nature] may bring about a useful application." AT&T, 172 F.3d at 1358-59, 50 USPQ2d at 1452. If the examiner determines that the claim does not entail the transformation of an article, then the examiner shall review the claim to determine if the claim provides a practical application that produces a useful, tangible and concrete result. In determining whether the claim is for a "practical application," the focus is not on whether the steps taken to achieve a particular result are useful, tangible and concrete, but rather that the final result achieved by the claimed invention is "useful, tangible and concrete." The claim must be examined to see if it includes anything more than a § 101 judicial exception. If the claim is directed to a practical application of the § 101 judicial exception producing a result tied to the physical world that does not preempt the judicial exception, then the claim meets the statutory requirement of 35 U.S.C. § 101. If the examiner does not find such a practical application, the examiner has determined that the claim is nonstatutory. (Guidelines, p. 20)*

The question is thus whether the final result achieved by the claimed invention satisfies all three criteria of being useful, and concrete, and tangible.

Furthermore, the useful, tangible, and concrete result must be recited in the claim itself, rather than addressed in specification.

Instant claims 1, 3-5, and 7-9 are drawn to a method for calculating a global hydrophobic moment of a tertiary protein structure. However, as claimed, the method does not produce a tangible result. For example, the method as claimed may take place entirely within the confines of a computer or a human mind without any communication to the outside world and without using or making available for use, the

results of the computation. In an embodiment of the instant set of claims, the "outputting" step may cause the result to be presented to a user in the form of a carrier wave, which, *per se*, is not statutory. Thus, the instant methods of the claims do not produce any tangible result.

The instant claims are also drawn to an apparatus and article of manufacture for optimizing the structure of a protein. Claims 14-15, 17, and 19-20 are directed to a "device" comprising "units" which appear to be instructions for performing method/program steps. Furthermore, the article of manufacture in claim 21 comprises computer readable media. The computer readable media comprise instructions for performing a method. Although the specification gives tangible examples of computer readable media (see page 12), the method performed by the computer and computer readable media does not produce a tangible result.

Consequently, with regard to all claims, the method to be performed does not produce a tangible result. For example, the method as claimed may take place entirely within the confines of a computer without any communication to the outside world and without using or making available for use, the results of the computation to a "user" (i.e. one performing the method). Thus, the instant methods of the claims do not result in a transformation of an article to a different state or thing, nor do they produce any tangible result, therefore the claims are directed to nonstatutory subject matter.

Response to Arguments:

Applicant's arguments filed 7 May 2008 have been fully considered but they are not persuasive. Applicant argues that the amendment to the instant set of claims of

outputting the global linear hydrophobic moment to at least one of a user, display, and one or more additional computers on a network overcomes the rejections of record. However, this argument is not persuasive because the global linear hydrophobic moment can still be output to one or more additional computers on a network and still not be accessible to a user.

***Claim Rejections - 35 USC § 112***

The rejections of claims 1, 3-5, 7-9, 14-15, 17, are 19-21 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in view of amendments filed on applicant on 7 May 2008.

***Claim Rejections - 35 USC § 103***

**The following 35 U.S.C. 103 Rejection is reiterated:**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3-5, 7-9, 14-15, 17, and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eisenberg et al. [Nature, volume 299, 1982, pages 371-274] in view of Silverman [PNAS; April 24, 2001; volume 98, pages 4996-5001].

Claim 1 is drawn to a method for calculating a global hydrophobic moment of a tertiary protein structure comprising a plurality of residues, the method comprising the steps of:

- calculating a centroid of residue centroids;
- using the centroid of residue centroids as a spatial origin of a global linear hydrophobic moment;
- calculating a first-order hydrophobic moment;
- enhancing correlation between residue centroid magnitude and residue solvent accessibility, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a distance metric;
- using the first order hydrophobic moment and the enhances correlation between residue centroid magnitude and residue solvent accessibility to define a global linear hydrophobic moment, wherein each of the residue centroids contributes a magnitude and direction to the global hydrophobic moment;
- using the global linear hydrophobic moment to characterize an amphiphilicity of a tertiary protein structure; and
- outputting the global linear hydrophobic moment to at least one or a user, a display, a memory and one or more additional computers on a network.

Claim 14 is drawn to the same subject matter as claim 1 wherein an apparatus is used fro executing the method.

Claim 21 is drawn to the same subject matter as claim 1 wherein an article of manufacture is used for calculating a global hydrophobic moment of a tertiary protein structure.

Claims 3-4 and claims 19-20 are further limiting with the additional limitations that the correlation between the residue centroid magnitude and the residue solvent accessibility is enhanced by using an ellipsoidal metric and a solvent accessibility metric, respectively.

Claim 5 and claim 15 are further limiting with the additional limitation that the centroid of residue centroids represents a geometric center of the tertiary protein structure.

Claims 7-9 and claim 17 are further limiting with the additional limitations that the global linear hydrophobic moment characterizes the magnitude of amphiphilicity, direction of amphiphilicity, and identification of functional regions in the tertiary protein structure, respectively.

The article of Eisenberg et al. studies use of a first order helical hydrophobic moment to measure the amphiphilicity of a helix.

The abstract on page 371 of Eisenberg et al. quantifies the mean hydrophobic moment as a vector sum of all of the first order hydrophobic moments of the residues constituting the helix.

Figure 1 of page 372 of Eisenberg et al. illustrates a vector sum for a helix to determine a global (i.e. mean) hydrophobic moment for a protein helix. Each residue in the helix contributes a magnitude and direction of the global hydrophobic moment.

Figure 2 on page 374 of Eisenberg et al. plots the hydrophobic moments of helices of different proteins as a function of the degree of hydrophobicity/amphiphilicity of each of the helices in the study.

Figure 1 is also an output of the global linear hydrophobic moment for an alpha helix.

However, Eisenberg et al. does not use residue centroids as the origins in the hydrophobic moment calculations (instead, alpha carbons are used as reference points), Eisenberg et al. does not show correlation enhancement between residue centroid magnitude and solvent accessibility, and Eisenberg et al. does not show the computer hardware and software limitations of the instant claims.

The article of Silverman, "Hydrophobic moments of protein structures: Spatially profiling the distribution," describes how to calculate moments of tertiary protein structures.

In equation [12] on page 4997 of Silverman,  $r_i$  is the vector pointing to the centroid of residue  $i$  while  $r_c$  is the vector pointing to the centroid of the entire protein molecule (i.e. the geometric center of the protein).

In equation [13] on page 4998 of Silverman, a first order hydrophobic moment imbalance about the entire protein is derived, accounting for hydrophobicity and solvent accessible surface area. Each centroid of every protein residue contributes to this global moment.

In equations [13] and [14] on page 4998 of Silverman, distance metrics, ellipsoidal metrics, and a solvent accessibility are all used to enhance the centroid magnitude.

Figure 6 on page 5000 of Silverman shows how an arm of the protein can be identified as it falls outside the ellipse characterizing the hydrophobic moment of the protein.

Pages 4998-5000 of Silverman illustrate the computation of a hydrophobic moment for entire proteins.

Additionally, page 4998, column 2 teaches the obtaining of protein structures from the Internet, and page 5000, column 2, paragraph 2 teaches obtaining protein structures from the PNAS website.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the helical hydrophobic moment study of Eisenberg et al. by use of the hydrophobic moment study of Silverman wherein the motivation would have been that using residue centroids instead of atomic points yields a more ideal overall shape and moment of the protein (see first full paragraph of column 1 on page 4998 of Silverman). Additionally, automation of the process of Eisenberg et al. on the internet provides a faster and more efficient means of executing the claimed invention.

Response to Arguments:

Applicant's arguments filed 7 May 2008 have been fully considered but they are not persuasive.

Applicant argues on page 9 of the Remarks that Silverman teaches second and zero order hydrophobic moments and not first order hydrophobic moments. This argument is not persuasive because Eisenberg et al. teaches first order hydrophobic moments and the combination of Eisenberg et al. and Silverman are used for the instant obviousness prior art rejection. Consequently, the combination of Silverman and Eisenberg et al. teaches all of the limitations of the amended set of claims.

***Conclusion***

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices

published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)).  
The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/RSN/  
Russell S. Negin, Ph.D.  
24 July 2008

/Marjorie Moran/  
Supervisory Patent Examiner, Art Unit 1631